

REMARKS

Applicant respectfully requests entry of the amendments and reconsideration of the claims. Applicants have amended claims 1 and 25. Support for the amendments can be found throughout the specification. No new matter has been added by the amendments. Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 102(e), 103(a), and 112, first and second paragraphs.

Information Disclosure Statement

Applicant had previously submitted Moncada et al. (*Pharmacol. Rev.*, 1991) in an information disclosure of November 1, 2004. However, the Form 1449 only recites pages 109-115, and the document submitted was only the partial reference as cited. In the information disclosure filed concurrently with this response, the entire article is submitted.

Rejection under 35 U.S.C. § 112, First Paragraph

The Examiner rejects claims 1-3 and 19 under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description. Applicant has amended claim 1 to delete “or is at risk of developing Type II diabetes”. Applicant respectfully requests removal of this rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claim 25 under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. Specifically, the Examiner contends that the term “kit” lacks antecedent basis. Applicant has amended claim 25 to recite “...wherein the method comprises administering...” Applicant respectfully requests removal of this rejection.

Rejection under 35 U.S.C. § 102(e)

The Examiner rejects claims 1, 3, and 19 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,165,975 (Adams et al.) as evidenced by U.S. Patent No. 6,887,872 (Nagy et al.). "Anticipation requires the presence in a single prior art reference disclosure of each and every

element of the claimed invention, arranged as in the claim." *Lindemann Mashinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *See also*, MPEP §2131. For rejections under 35 U.S.C. §102(e), the U.S. patent reference must support the claimed invention as required by 35 U.S.C. §112, first paragraph, in addition to having a right of priority to the earlier date under 35 U.S.C. §120 or §365(c). *In re Wertheim*, 646 F.2d 527, 537 (C.C.P.A. 1981); *see also*, MPEP §2136.03. Applicant respectfully traverses this rejection.

Claim 1 requires administration of a therapeutic nitric oxide donor compound to a patient with Type II diabetes. The '975 patent discloses, in the broadest description, treatment of patients with vascular conditions and specifically, erectile dysfunction (see, e.g., col. 4, lines 15-17 and claim 1 at col. 19, lines 44-47). The '975 patent does not teach administration of any compounds to patients with Type II diabetes. Thereby, the '975 patent does not disclose each and every element of amended claim 1. For at least this reason, Applicant respectfully asserts that the '975 patent does not anticipate pending claims 1, 3, and 19.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claims 1-3, 19, and 21-25 under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 6,165,975 (Adams et al.) in view of U.S. Patent No. 5,698,738 (Garfield) and U.S. Patent No. 5,561,165 (Lautt et al.). Applicant respectfully traverses the rejection.

To make a *prima facie* case of obviousness, the teachings of the prior art should have suggested the claimed subject matter to the person of ordinary skill in the art, and all the claim limitations must be taught or suggested in the references cited by the Examiner. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). As articulated by the Supreme Court, a combination is obvious if it is no more than the predictable use of known elements according to their established functions; and there was a reason to combine the known elements. *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007). To make a *prima facie* case of obviousness, "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art

elements in the manner claimed.” *Id.* The initial burden to make a *prima facie* case of obviousness is on the Examiner. *In re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993). Applicants submit that the Examiner does not make a *prima facie* case of obviousness, because all the limitations of the present claims are not taught by the combination of references cited in the Office Action.

Applicant respectfully asserts that the combination of the ‘975, ‘738, and ‘165 patents do not teach or suggest all of the claim elements, i.e., a connection between administration of a nitric oxide donor to increase insulin sensitivity. The Examiner cites the ‘738 patent as teaching the connection between nitric oxide pathways, diabetes, and hypertension. The Examiner specifically cites the recitation of a connection between nitric oxide and the pathology of other diseases, including diabetes (at col. 1, lines 56-60). At said recitation, the patentees cite Moncada et al. (*Pharmacol. Rev.*, 1991) in support of their statement of the connection between nitric oxide and the pathologies of other diseases. Moncada et al. do not discuss diabetes at all within the article (full article submitted concurrently with this response). In this context, the recitation to diabetes only pertains to the pathogenesis of vascular complications of diabetes—hypertension, atherosclerosis, and the like, and not the pathology of diabetes (Type I—insulin deficiency due to pancreatic β -cell destruction; Type II—peripheral resistance to insulin action and inadequate secretory response by pancreatic β -cells). "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. MPEP § 2141.02(VI); *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). The ‘738 patent does not make any connection between nitric oxide and insulin (secretion and/or resistance). For at least this reason, Applicant respectfully asserts that the ‘738 patent can only be viewed as linking nitric oxide with vascular complications of diabetes and not the pathology of diabetes itself.

Further, Applicants respectfully assert that the Examiner has not sufficiently established a reasoning for combining the ‘975 and ‘738 patents with the ‘165 patent. The ‘975 patent teaches nitric oxide donors and administration thereof. The ‘738 patent teaches the connection between nitric oxide and vascular pathology. However, the ‘165 patent teaches *diabetic neuropathies*, as

the Examiner states at page 11 of the office action. Applicant respectfully asserts that there is no motivation to combine the '975 patent about nitric oxide and the '738 patent teaching the connection between nitric oxide and vascular pathologies with a patent ('165) disclosing diabetic neuropathies. Applicant contends that there is no motivation to combine a reference regarding insulin sensitivity and diabetic neuropathies with a reference regarding vascular pathology.

Applicant respectfully asserts that the Examiner has not established a *prima facie* argument of obviousness for the administration of a nitric oxide donor to increase insulin sensitivity. Applicant respectfully asserts that there is no motivation to combine the '165 patent with the '738 and '975 patent. [A]n obviousness rejection where the relied upon references teach that all the aspects of the claims were individually known is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. MPEP § 2143.01(III); *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (Bd. Pat. App. & Inter. 1993); See also *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). Additionally, the references do not establish a connection between administering nitric oxide and a resultant increase in insulin sensitivity.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Rejection for Nonstatutory Obviousness-type Double Patenting

The Examiner rejects claims 1-3, 19, and 21-25 for alleged nonstatutory obviousness-type double patenting over claims 30-33 and 34-39 of copending application No. 10/761,596. U.S. Serial No. 10/761,596 is now abandoned. A notice of abandonment was mailed September 30, 2008. A copy is submitted with this response. Applicants respectfully request removal of this rejection.

Summary

In view of the above amendments and remarks, the applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance

U.S. Patent Application Serial No. 09/806,989
Amendment dated December 17, 2008
Reply to Final Office Action of July 24, 2008

Confirmation No. 7861

prosecution of this application, the Examiner is invited to telephone the undersigned at the below listed telephone number.

Respectfully submitted,

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Date: December 17, 2008



A handwritten signature in black ink, appearing to read "B. R. Dorn", written over a horizontal line.

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